Why Human Bone is More Prone to Fracture with Age

DOE-Supported Research Provides New Mechanistic Insights into Bone Aging

A collaboration involving MSD Scientists Robert Ritchie and Joel Ager, Postdoctoral Fellows Ravi Nalla and Jamie Kruzic, and John Kinney of Lawrence Livermore National Laboratory, has provided new and fundamental insights into the effects of aging on the human bone.

Aging-related changes to the musculoskeletal system are known to increase the susceptibility of bone to fracture, and, in the very elderly, to mortality. Traditional thinking concerning "bone quality" has focused on bone mass or bone mineral density (BMD) as a predictor of such fracture risk. However, there is mounting evidence that BMD may not be the sole factor responsible for aging-induced fracture risk. Thus there is increased interest in the fundamental understanding of bone toughness, and how this changes with age.

Techniques honed from decades of DOE supported research on advanced metals, ceramics and composites were applied to assess the fracture resistance of human cortical bone taken from cadavers ranging in age from 34 to 99 years. "Compact tension" specimens were machined from humeral bone and the loads required to initiate and propagate cracks were measured precisely. Three dimensional imaging of bone microstructure was performed by tomography using synchrotron X-rays at the Advanced Light Source, and at the Stanford Synchrotron Radiation Laboratory. Ultraviolet Raman spectroscopy was performed to assess changes in protein crosslinking at the nanoscale.

The group found that the resistance of bone to the initiation of cracks falls by 40% over the age range examined. Most strikingly, the ability of a bone to "resist" the growth of an existing crack falls essentially to zero over the same age range. X-ray tomography and vibrational spectroscopy studies revealed the mechanism underlying this effect. In bones of younger individuals, the researchers observed large (on the scale of tens of micrometers), unbroken regions of bone material acting like "bridges" spanning the cracks (analogous to steel rods in reinforced concrete). These "uncracked-ligament" bridges are somewhat like "zipper teeth," holding the crack together so it does not rip through the material (see Highlight 3-11). In bones from older individuals, however, the amount of such bridging was greatly reduced, explaining why older bone is less able to resist fracture. The Raman spectroscopy studies showed that the degree of cross-linking in the collagen molecules in the bone changes with age and is correlated to the changes in the fracture behavior. Thus, nanometer scale changes due to aging can lead to deterioration of the fracture properties at a macro-size scale.

Although supported by NIH, this study applied a wide range of techniques—mechanical testing, tomography and spectroscopy—that had been developed for the study of traditional engineering materials through many years of support from the DOE Materials Sciences Division. It demonstrates that these techniques can be successfully applied to the study of biological materials as well and to developing biomedical advances that can help understand and mitigate the effects of aging, injury and disease.

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